Fish Poisoning: A Problem in Food Toxication

ALFRED F. BARTSCH and EARL F. MCFARREN[1]

INTEREST IN POISONOUS FISHES has intensified greatly in recent years. World War II brought many Americans and Europeans to tropical areas of the world where fish poisoning is common. Also, interest in the welfare of native populations of the Pacific islands has developed widely, and there is an impression that fish poisoning is increasing. In spite of an extensive literature, there is considerable confusion on the subject.

Some marine organisms are dangerous because of their venomous stings or bites, while others are poisonous to eat. Among the latter are shellfish of several kinds, including mussels, clams, and oysters. Some fin fishes also are poisonous to eat. They are intrinsically poisonous and, like the toxic shellfish, do not produce their undesirable effects through bacterial spoilage. Such fishes are the subject of this paper. The fish poisoning problem is especially insidious because of its inconsistencies. For example, a species is not always poisonous and therefore summarily rejected; it may be eaten safely in some localities and not in others, or at some times of year and not at others. Large specimens, otherwise attractive as food, are believed more likely to be dangerous than smaller ones.

Different from the usual fish poisoning episodes is Haffs' disease noted among fishermen along the Baltic Sea coast of East Prussia and at Lake Ysmen in Sweden (Schwimmer and Schwimmer, 1955). The more than a thousand victims had consumed eels, eel livers, and a few other kinds of fish. Animals that ate the fish also became ill and died. Selenium was once thought to be involved in the etiology (Berlin, 1948); toxic blue-green or other algae in the food chain of the fish have been suspected, also.

Another atypical episode occurred recently along the shores of a small bay in Japan, where local people were poisoned by eating fish and shellfish. Their affliction has been called Minamata disease after the name of the bay. Investigation[2] has shown the causative agent to be a mercury compound accumulated in the tissues of the sea food. Mercury was reaching the bay as a component of wastes discharged from a vinyl chloride manufacturing plant. Remedial waste handling measures recently installed at the plant, coupled with a ban on fishing, have been fairly successful in curbing the number of new cases.

Typical poisonous fishes are limited principally to the warm seas lying mostly between 30° N. and 30° S. They are most numerous around isolated islands far from continental shores, such as those of Micronesia, Melanesia, and Polynesia. In the Caribbean, they are common around the West Indies.

In spite of the numerous shore and reef fishes available as food in the tropic seas, potential toxicity is a deterrent to commercial harvest as well as to use by native populations. Because recognition of poisonous specimens presently requires tedious and time-consuming techniques, a tremendous poundage of potentially useful fish cannot be brought to market nor used freely to meet the food needs of local populations. This problem is far from solution at the present time.

HISTORY

Existence of poisonous fishes became much better known during World War II. They are believed to have killed more than 400 Japanese military personnel in Micronesia alone (Halstead, 1959). American military manuals warned against poisonous fishes, one (Smithsonian In-

[1] Robert A. Taft Sanitary Engineering Center, Public Health Service, Department of Health, Education, and Welfare, Cincinnati, Ohio. Manuscript received February 21, 1961.

[2] Personal communication from Leonard T. Kurland, M.D., Dr. P. H., Chief, Epidemiology Branch, National Institute of Neurological Diseases and Blindness, Public Health Service, Bethesda, Md.

stitution, 1944) stating: "All these fish [with poisonous flesh] lack ordinary scales such as occur on bass, grouper, and sea trout. Instead, these poisonous fish are covered with bristles or spiny scales, strong sharp thorns, or spines, or are encased in a bony box-like covering. Some of these have naked skin, that is, no spines or scales. Never eat a fish that blows itself up like a balloon." Subsequent military literature has been revised in the light of more recent knowledge. Nevertheless, some service men by mistake have partaken of poisonous fishes, with painful result. A number of cases have been cited in the literature (Halstead, 1951, 1954). U. S. occupation or trusteeship of many Pacific islands has emphasized to Americans the problem of poisonous fishes.

Centuries ago, however, poisonous fishes already had made a mark in history. Captain Cook and several officers of HMS "The Resolution" almost ended their voyage in 1774 because they were poisoned from eating a puffer obtained from natives in New Caledonia (Courville *et al.,* 1958). Down through the years many articles have been written by persons whose scientific interests or economic pursuits have brought them in contact with the problem. Their reports of case histories invoke a healthy respect for the dangers of fish poisoning. The following examples show why.

Ciguatera

In May of 1956 in a rooming house at Fort Lauderdale, Florida, a fine-looking 6½-lb. barracuda (*Sphyraena* sp.) was taken from a deep freeze, where it had been kept since capture the day before, and prepared for the evening meal (Paetro, 1956). It was served to five guests and all of them became ill within 2 hr. Three of the victims were hospitalized. Recovery took from 2 to 6 weeks, with symptoms persisting in one case almost 4 months.

Puffer Poisoning

At about the same time, a 65-year-old tourist in south Florida ate the liver of a puffer (*Sphraeroides testudineus* Linnaeus) common in the area (Benson, 1956). Symptoms appeared within 5 min. and the victim died 45 min. after eating the fish.

Moray Eel Poisoning

At Saipan during May of 1949 several Filipinos captured a 6-ft. moray eel (*Gymnothorax flavimarginatus* [Ruppel]) which they dressed, sliced into steaks, and cooked, including the head (Khlentzos, 1950). All 57 persons who ate the fish became sick. After 3 days, 50 who were bedridden and unable to talk were taken on litters to the Saipan dispensary, and the sickest 17 of this group were moved by air to the general hospital at Guam. Two died, one after 14 days and the other after 20 days. In the others, recovery was prolonged, in some cases taking 2 months or more.

Scombroid Poisoning

In Hiroshima during the winter of 1953, three households bought dried mackerel pike (*Cololabis saira* Brevoort), known locally as "samma sakuraboshi," from a peddler (Kawabata *et al.,* 1955*a*). After broiling, the fish was eaten by 11 persons, who within 2½ hr. developed flushing of the face and upper half of the body, palpitation, severe headache, dizziness, and nausea. Fourteen outbreaks of this type of poisoning, involving 1,215 persons, occurred in Japan during a 2-yr. period ending October 1954 (Kawabata *et al.,* 1955*a*). In this fairly mild poisoning, victims commonly recover in a day or less.

STATUS OF FISH POISONING IN THE MARSHALLS

Although many species of fishes known to be poisonous occur in tropical areas, much attention has centered on the Marshall Islands. Starting in 1924, Matsuo, a Japanese medical officer, studied the poisonous fishes at Jaluit Atoll for a number of years (Matsuo, 1934). He listed 36 of 180 species there as poisonous. In 1941, Hiyama studied the fishes at Jaluit and wrote a superbly illustrated report (Hiyama, 1943). At that time, other island groups in the Pacific seemed little involved with fish poisoning, and even now Jaluit is considered by some as the center of the problem.

Scientific interest in the United States was stimulated by outbreaks in the Line Islands involving 95 persons out of a population of 224. Subsequent studies by Halstead and his asso-

ciates (Halstead, 1959; Halstead and Bunker, 1954) led them to conclude that fish poisoning at Midway, Johnston, and the Line Islands rose to a peak in 1947 and has since declined. As recently as 1958, however, Marshallese of Majuro and Jaluit atolls believed that fish poisoning was still increasing and expressed their concern to the Trust Territory. As a result, an exploratory survey was made at request of Trust Territory officials to accomplish several objectives, including the following:

1. Define the extent of the fish poisoning problem in the Marshall Islands (especially at Majuro and Jaluit) in terms of human morbidity, and other epidemiologic characteristics available, in relation to the fishes involved and their toxicology.
2. Ascertain if poisonous fishes are currently available in the area for human consumption.
3. Collect sufficient information to permit development and proposal of a long-range definitive study of the problem, if indicated.

Epidemiological Characteristics

Epidemiological data came from reviews of Out-Patient Department (OPD) records of the Marshall Islands Memorial Hospital on Uliga Island of Majuro Atoll, questionnaires distributed in the Majuro area, and house-to-house surveys at a number of islands. Included were Darrit, Uliga, and Majuro islands of Majuro Atoll, and Jabor and Imroij islands of Jaluit Atoll. Survey conditions at Jaluit were difficult and less than satisfactory because of appalling damage and disruption caused by a recent typhoon.

OPD summaries for 1955–57 yielded information on the number of persons with fish poisoning and those with a diagnosis of gastrointestinal illness (Table 1). Respiratory illnesses, constituting a group of diseases unrelated to fish poisoning, were examined for comparison. During this period visits increased 60 per cent, whereas fish poisoning and gastrointestinal illnesses increased two to three times. Trends in incidence of respiratory illnesses also showed only a very slight increase and thus no apparent relationship to the other two. Information on population change that would be reflected in these trends was not at hand, but it was thought to be slight. There appears to be no reciprocal relationship between gastrointestinal illness and fish poisoning, suggesting that the former had stayed near its expected level and was not being misdiagnosed as fish poisoning. However, parallelism of the trend curves raises the question of whether fish poisoning may be mistaken for gastrointestinal illness. In August 1957 Trust Territory medical personnel distributed a questionnaire to all atoll dispensaries in the Marshalls. Use of this form identified the victim, described symptoms, treatment, and outcome, and gave the name, origin, and mode of handling of the fish. It is believed that such information has not been available in the past to students of the problem. Questionnaires for the area accessible to the hospital were selected as a comparable group susceptible of analysis. The following information is based on 91 cases.

Twenty-seven species of fishes were implicated in these outbreaks. Eleven cases were caused by red snapper (*Lutjanus vaigiensis* Quoy and Gaimard), 8 by rock cod (*Epinephelus fuscoguttatus* Forskal), 5 by mijmij (*Lethrinus microdon* Cuvier and Valenciennes), 4 by each of two other species, 3 by one species, 2 by each of seven, and each of the remainder by separate species.

The victims were in the following age groups:

AGE GROUPS	NO. OF PATIENTS	PER CENT OF TOTAL NUMBER	PER CENT OF TOTAL DISTRICT POPULATION OF AGE GROUP
0–5	5	8	39
6–14	2		
15–44	73	80	39.4
45+	10	11	21.4
unknown	1	–	–

The small number of victims under 14 yr. is striking, 8 per cent, since this age group constitutes 39 per cent of the population. Because common varieties of gastrointestinal diseases usually involve children more frequently than adults, these reported illnesses probably are not classical enteritis. Based on a year's data and a population of about 2,500, the fish poisoning attack rate was 9.3 per cent.

Of the persons who partook of the fishes in question, 76 per cent became ill; 24 per cent of them were hospitalized. The onset of symptoms ranged from 30 min. to 12 hr. after eating, with a median of 3 hr. Symptoms reported for the 91 victims were:

SYMPTOM	NO. OF PERSONS	PER CENT
numbness and tingling	52	57
muscle aches	9	10
nausea	45	49.5
vomiting	50	55
diarrhea	60	66
abdominal pain	54	59
weakness	27	30
dyspnea	8	9

In some island areas the view is expressed that only fishes taken on the outer reefs are likely to be toxic; elsewhere the view is reversed. Here 72 per cent came from the lagoon, 18 per cent from the reef. Obviously, selecting fish by place of capture is poor protection against poisoning. Although some fish were consumed within 30 min. of capture, others were kept for as long as 48 hr., so that spoilage seems a distinct possibility in some cases; 46 per cent were prepared by evisceration, but 40 per cent were not cleaned at all. Uncleaned fish commonly are eaten in their entirety.

The erratic distribution of fish poisoning among Pacific island groups still challenges interpretation. There is little reason to believe that fish taken in other coral reef areas are handled in a significantly different manner or with better sanitation than in the Marshalls. It is assumed that they also are left routinely at air temperature until consumed and that the extent of cleaning varies widely. Accordingly, fish handling is not considered a significant factor, and it is more likely that distribution of poisoning reflects the intrinsic toxicity of the fishes, acquired in the ocean or reef environment from which they came.

During recent years fish poisoning has been common in the vicinity of Majuro Atoll, but absent at Koror in the Palau Islands lying at the same latitude 2,000 mi. west (Table 1). In public health statistics for the entire Trust Territory, fish poisoning episodes are included in the accident category. The accident rate in the Marshalls is higher by at least 50 per cent than the rate for the entire Trust Territory. These pieces of information, though limited, still suggest a greater prominence of fish poisoning in the Marshalls than elsewhere.

Survey Information

At Rita and Uliga islands, 35 families with a total membership of 375 persons were visited to obtain information on their experiences with fish poisoning during the previous year. During the questioning it became obvious that at least some persons differentiated common diarrheal disease from fish poisoning. Fourteen per cent

TABLE 1

SUMMARY OF MARSHALL ISLANDS MEMORIAL HOSPITAL DISPENSARY (OPD) REPORTS

YEAR	TOTAL OPD PATIENT VISITS	GASTROINTESTINAL ILLNESSES	FISH POISONING	RESPIRATORY ILLNESSES
1955, last half	3,439	97	22	862
1956	7,696	190	100	2,304
1957	11,686	791	211	1,615

SUMMARY OF KOROR HOSPITAL (PALAU ISLANDS) DISPENSARY (OPD) INFORMATION

1956	23,604	1,105	NR*
1957	31,355	1,220	NR
1958 (Jan.–Apr.)	9,143	511	NR

* NR=No cases reported.

of the persons questioned reported that they had been victims of fish poisoning; 6 per cent were hospitalized and the other 94 per cent reported to the OPD for treatment.

Rock cod (*Epinephelus fuscoguttatus* Forskal), red snapper (*Lutjanus vaigiensis* Quoy and Gaimard), mullet (*Chelon vaigiensis* Quoy and Gaimard), and rabbitfish (*Siganus puellus* Schlegel) were each involved in only three incidents although many families normally ate these fish. Similar data on Majuro Island gave an attack rate of 15 per cent for the previous year. Here the implicated fishes were rock cod (probably *Anyperodon leucogrammicus* Cuvier and Valenciennes), scavenger (*Lethrinus* sp.), and parrotfish (*Callyodon pulchellus* Ruppel).

Information obtained from native populations is filled with inconsistencies and is difficult to interpret. In some cases a fish pointed to as toxic would be accepted readily and used as food. Taboos and customs add confusion. Much difficulty results from faulty communication and the language barrier, especially as to names of fishes. Toward alleviating this problem, it was necessary to translate Marshallese names to English and technical names, although this did not solve the problem completely.

Availability of Poisonous Fishes

In most efforts to ascertain the presence of poisonous fishes in a given area, it has been common practice to capture as many fish as possible and subject them to animal assays. Fish tissues were fed to cats, rats, mice, chickens, mongooses, and other animals, or tissue extracts were injected intraperitoneally into mice. Obtaining an understanding of the logistic problems to be faced in a future on-the-spot intensive study of the problem was a main reason for collecting fishes and undertaking exploratory tests to determine their toxicity. It provided a first-hand, thorough, personal "feel" for the obstacles to be encountered by future investigators, and suggested solutions. Concurrently, some idea of the availability of poisonous fishes was obtained.

Fishes were taken at Majuro and Jaluit atolls by spearing, poisoning, or angling, and a few were obtained by Marshallese fishermen using throw nets. There were various collecting stations representing lagoon, outer reef, and oceanic habitats. Of the many fishes collected, 66 specimens representing 41 species from Majuro Atoll and 41 specimens representing 26 species from Jaluit Atoll were selected for study. Some were assayed by mouse injection, others by both mouse injection and cat feeding. The mouse assay method is the same as used in assaying for paralytic shellfish poison (McFarren, 1959). It is known to be applicable to puffer fish poison (Hori, 1957; Hashimoto and Migita, 1951), and other investigators (Hiyama, 1943; Halstead and Schall, 1955) have used a similar method for other species of fishes and presumed it to be applicable.

In our tests each of three mice were injected with 1 ml. of the supernatant fluid obtained by centrifuging an aqueous acid extract of ground whole fish, muscle tissue, or visceral organs such as liver, ovaries, or intestines. Mouse responses were observed thereafter for at least 18 hr.

Fishes were prepared for cat-feeding tests by cooking small pieces of muscle or other organ for 30 min.; 100 g. of such material offered to a mature cat previously fasted for 24 hr. was always eaten readily; occasionally 200 g. were fed without difficulty. Puffers (*Tetraodon hispidus* Linnaeus), although available, were not tested with cats because positive mouse response was sufficient indication that fed cats would become ill (Murtha *et al.*, 1958).

Test results are summarized in Table 2. In all, 171 preparations were used, 124 extracts from 98 specimens injected into mice and 47 portions from 43 specimens fed to cats. These represented 51 different species. Of this total only 3 specimens of puffer (*Tetraodon hispidus* Linnaeus) were clearly toxic to mice, while 4 specimens—3 of red snapper (*Lutjanus gibbus* Forskal) and 1 scavenger (*Lethrinus miniatus* Bloch and Schneider)—caused illness in cats. On the basis of the tests used, only 7 of 98 specimens comprising 3 of 51 species tested could be considered potentially toxic to humans. Actually, the muscle of only 2 of the puffers was found toxic and the viscera of the third only mildly toxic. The muscle of another red snapper and of 6 other species of the snapper family (Lutjanidae) were nontoxic by cat-feeding test (Table 2).

TABLE 2

Summary of Bioassay Data for Specimens from Majuro and Jaluit Atolls

SPECIMEN NO.	NAME	PORTION TESTED	MOUSE RESPONSE*	CAT RESPONSE*
1	*Gymnothorax pictus* Ahl	viscera	—	NT
		muscle	—	NT
2	*G. pictus* Ahl	whole	—	NT
3	*G. pictus* Ahl	ovaries, viscera	—	NT
		muscle	—	NT
11	*Rhinecanthus aculeatus* (Linnaeus)	whole	—	NT
12	*Chelon vaigiensis* (Quoy & Gaimard)	whole	—	NT
12A	*C. vaigiensis* (Quoy & Gaimard)	whole	D	NT
14	*Tetraodon hispidus* Linnaeus	muscle	—	NT
		liver	D	NT
		viscera	+	NT
15	*Euthynnus alteratus* (Rafinesque)	muscle	—	NT
		liver	D	NT
16	*Caranx melampygus* Cuvier	muscle	—	NT
		viscera	—	NT
17	*Sphyraena barracuda* (Walbaum)	muscle	—	NT
18	*S. forsteri* Cuvier and Valenciennes	muscle	—	NT
19	*Variola louti* (Forskal)	muscle	—	NT
20	*V. louti* (Forskal)	muscle	—	NT
21	*V. louti* (Forskal)	viscera	—	NT
22	*Epinephelus merra* Bloch	whole	—	NT
23	*E. merra* Bloch	muscle	D	NT
24	*Halichoeres trimaculatus* (Quoy & Gaimard)	whole	—	NT
25	*Mulloidichthys samoensis* (Gunther)	whole	D	NT
		viscera	D	NT
26	*Lutjanus monostigmus* (Cuvier & Valenciennes)	whole	—	NT
		viscera	—	NT
27	*Arca* sp. (ark shellfish)	whole	—	NT
28	*Echidna nebulosa* (Ahl)	whole	—	NT
29	*Scarus jonesi* (Streets)	muscle	—	NT
		viscera	—	NT
30	*S. harid* Forskal	muscle	—	NT
		viscera	+	NT
31	*Hepatis triostegus* (Linnaeus)	whole	—	NT
32	*Hyporhamphus laticeps* (Gunther)	whole	—	NT
33	*Epinephelus macrospilos* (Bleeker)	viscera	D	NT
34	*Trochus* sp. (trochus shellfish)	whole	+	NT
		viscera	+	NT
35	*Anyperodon leucogrammicus* (Cuvier)	viscera	—	NT
36	*Chaetodon ephippium* Cuvier	whole	—	NT
37	*C. auriga* Forskal	whole	—	NT
38	*Holocentrus praslin* (Lacepede)	whole	—	NT
39	*Acanthurus leucosternon* Bennett	whole	—	NT
40	*Abudefduf septemfasciatus* Cuvier & Valenciennes	whole	—	NT
41	*Belone platyura* Bennett	whole	—	NT
42	*Gymnothorax flavimarginatus* Ruppel	whole	—	NT
43	*Acanthocybium solandri* (Cuvier)	muscle	—	NT
		viscera	D	NT
44	*Lutjanus gibbus* (Forskal)	muscle	D	NT
		viscera	D	NT
45	*Epinephelus fuscoguttatus* (Forskal)	muscle	—	—
		viscera	D	NT
46	*Lutjanus gibbus* (Forskal)	muscle	—	NT
		viscera	D	NT

TABLE 2—*Continued*

SPECIMEN NO.	NAME	PORTION TESTED	MOUSE RESPONSE*	CAT RESPONSE*
46A	*L. gibbus* (Forskal)	muscle	—	NT
46B	*L. gibbus* (Forskal)	muscle	—	NT
46C	*L. gibbus* (Forskal)	muscle	—	—
47	*L. kasmira* (Forskal)	whole	—	NT
48	*Epinephelus kohleri* Schultz	whole	—	NT
49	*Turbo* sp. (top shellfish)	whole	D	NT
51	*Aprion virescens* Valenciennes	viscera	—	—
52	*Euthynnus pelamis* (Linnaeus)	viscera	—	NT
53	*Trachinotus bailloni* (Lacepede)	muscle	—	NT
54	*Germo alalunga* (Bonnaterre)	muscle	—	NT
55	*Plectropomus truncatus* Fowler	muscle	D	—
56	*Lutjanus* sp.	ovaries	—	NT
		gills, viscera	D	NT
57	*Conomurex* sp.	whole	D	NT
58	*Lutjanus gibbus* (Forskal)	muscle	D	NT
59	*Abudefduf saxatilis* (Linnaeus)	muscle	—	NT
60	*Chelon vaigiensis* (Quoy & Gaimard)	muscle	D	NT
61	*Mulloidichthys samoensis* (Gunther)	muscle	D	NT
62	*Lutjanus vaigiensis* (Quoy & Gaimard)	whole	D	NT
63	*Tetraodon hispidus* Linnaeus	muscle	++	NT
		liver	+	NT
64	*Epinephelus* sp.	broth	D	—
65	*Scarus* sp.	muscle	—	NT
66	*Gymnothorax pictus* Ahl	muscle	—	—
67	*Epinephelus fuscoguttatus* (Forskal)	muscle	—	—
		fat around viscera	—	NT
69	*Lutjanus gibbus* (Forskal)	muscle	NT	+
70	*Sphyraena barracuda* (Walbaum)	muscle	—	—
71	*Lutjanus monostigmus* Cuvier & Valenciennes	muscle	—	—
72	*Gerres argyreus* (Bloch & Schneider)	muscle	—	—
73	*Lutjanus* sp.	muscle	—	—
74	*Lethrinus miniatus* (Forster)	muscle	—	+
75	*Tetraodon hispidus* Linnaeus	muscle	++	NT
80	*Acanthocybium solandri* (Cuvier)	muscle	—	—
		liver	—	NT
81	*Euthynnus alteratus* (Rafinesque)	muscle	—	—
		liver	—	NT
82	*Epinephelus* sp.	muscle	—	—
83	*Euthynnus alteratus* (Rafinesque)	muscle	—	NT
84	*Aprion virescens* Valenciennes	muscle	—	—
85	*Plectropomus truncatus* Fowler	muscle	—	—
86	*Sphyraena barracuda* (Walbaum)	muscle	—	—
		ovaries, liver	—	—
87	*Lutjanus gibbus* (Forskal)	muscle	—	—
88	*Hepatis triostegus* (Linnaeus)	whole	—	—
89	*Mulloidichthys samoensis* (Gunther)	muscle	—	NT
90	*Kyphosus cinerascens* (Forskal)	muscle	—	—
		viscera	D	NT
91	*Lutjanus gibbus* (Forskal)	muscle	—	+
92	*Sphyraena barracuda* (Walbaum)	muscle	—	—
93	*Epinephelus fuscoguttatus* (Forskal)	muscle	—	—
94	*Caranx lugubris* Poey	muscle	—	—
95	*Variola louti* (Forskal)	muscle	—	—

TABLE 2—*Continued*

SPECIMEN NO.	NAME	PORTION TESTED	MOUSE RESPONSE*	CAT RESPONSE*
96	*Elagatis bipinnulatus* (Quoy & Gaimard)	muscle	—	—
97	*Lutjanus kasmira* (Forskal)	muscle	—	NT
98	*L. gibbus* (Forskal)	muscle	—	++
99	*Plectropomus oligacanthus* Bleeker	muscle	—	—
100	*Variola louti* (Forskal)	muscle	—	—
101	*Aprion virescens* (Valenciennes)	muscle	—	—
102	*A. virescens* (Valenciennes)	muscle	—	—
103	*Lethrinus* sp.	muscle	—	—
104	*L. miniatus* (Schneider)	muscle	—	—
105	*L. miniatus* (Schneider)	muscle	—	—
106	*Caranx melampygus* Cuvier & Valenciennes	muscle	—	—
107	*C. melampygus* Cuvier & Valenciennes	muscle	—	—
108	*Grammatorcynus bilineatus* (Ruppel)	muscle	—	—
109	*G. bilineatus* (Ruppel)	muscle	—	—
110	*Elagatis bipinnulatus* (Quoy & Gaimard)	muscle	—	—
111	*Neothunnus albacora macropterus* (Temminck & Schlegel)	muscle	—	—
112	*N. sexfasciatus* (Quoy & Gaimard)	muscle	—	—
113	*Caranx melampygus* Cuvier & Valenciennes	muscle	—	—
		total 126		

* —=negative
+=positive
D=toxicity doubtful
NT=not tested

None of the specimens found toxic by cat test gave a clearcut indication of toxicity when injected into mice. Hashimoto (1956) found a similar relationship with barracuda (*Sphyraena picuda* Bloch and Schneider). When mice were injected with aqueous extract, or even when fed the muscle, their response was very slight, whereas cats became severely ill or died after eating. Hashimoto also showed that the toxin in barracuda apparently is fat-soluble, because it could be extracted with ether. In Hawaii, Banner and Boroughs (1958) studied the toxin from a snapper (*Lutjanus bohar* Forskal) and found it insoluble in water but soluble in 90 per cent ethanol and some other solvents. Essentially similar characteristics were found by McFarren and Bartsch (1960) for the toxins of red snapper (*Lutjanus gibbus* Forskal) and a scavenger (*Lethrinus miniatus* Bloch and Schneider) from Jaluit Atoll. They also found that such poison can be assayed successfully by intraperitoneal injection of mice, using the oily residue obtained by concentration of an ethyl ether extract. All of these observations indicate that water extraction of macerated fish tissues, followed by centrifuging and intraperitoneal injection of the supernatant into mice, cannot be a valid test. Prompt positive mouse responses, when they occur, apparently result from toxic substances suspended or emulsified in the extract. Unfortunately, therefore, published data on distribution of ciguatera-producing fishes and their toxin intensity based on the customary mouse test are subject to question.

There can be no doubt, however, that some poisonous fishes are present in Majuro and Jaluit atolls. This has been demonstrated by assay for the poison of puffers (*Tetraodon hispidus* Linnaeus), red snappers (*Lutjanus gibbus* Forskal), and scavengers (*Lethrinus miniatus* Bloch and Schneider). In addition, information from the literature (Hiyama, 1943) and from questioning local populations implicate the last two in poisoning episodes. The puffer, of course, is not used as food, and considerable selectivity is exercised in taking other fish for consump-

tion. Even so, toxic specimens seem less common than findings of others would lead one to believe.

Are More Species Becoming Toxic?

During conversations and surveys among the Marshallese, it was often heard that a given species had become toxic only recently and that more kinds of fishes are toxic now than in the past. Information from the present study was examined in relation to that obtained by Japanese workers (Matsuo, 1934; Hiyama, 1943) at Jaluit Atoll in 1934 and 1941. Some general indication of the situation was obtained, in spite of the necessity to use Marshallese names which apparently are not only inconsistent but are applied to more than a single species. Accordingly, both the Marshallese name and the best judgment of the technical equivalent are given in Table 3.

Obviously, these earlier and later data are not strictly comparable, because of method of collection and the profound social, economic, and occupational changes among the Marshallese since 1941. Nevertheless, it is interesting that the number of implicated fishes at Jaluit has changed only from 18 to 22 during the 24-yr. period. The number of species implicated at Majuro was 23, but composition at one place varied somewhat from the other, so that Jaluit and Majuro together had 32. Of the 91 poisoning episodes cited earlier, the principal fishes concerned were already toxic in 1934 or 1941, as shown by the following list of those causing two or more incidents:

It is concluded that there is no striking evidence that species that have been untainted in the past have suddenly become poisonous.

Undoubtedly, throughout the course of history, persons involved in fish poisoning have wondered how fishes become toxic. Numerous ideas have been expressed—from fish eating manchineel berries dropping onto the water to uptake of copper from natural deposits or sunken ships. Now it seems generally agreed that fishes become poisonous through influences existing in the reef environment. This has been stated many times, but never so clearly or in such logical sequence of steps as by Randall (1958) in a recent review of ciguatera: (a) toxin must originate in the environment because only fishes in a restricted area are toxic, while those of similar size elsewhere are not; (b) in affected areas not all species are toxic, and, because food and feeding habits are the principal variables, their food is a likely source of toxin; (c) the food is probably benthic, because toxic specimens of a species occur with it but not in open seas where only plankton are available; (d) if the benthic food is algae, it must be small to accommodate the delicate mouth structures of some poisonous fishes; (e) blue-green algae, sometimes toxic, are suspect; (f) violently poisonous large predaceous fishes presumably accumulate toxin from their less toxic prey, and they can retain the toxin for a long time after being separated from that source; (g) the course of events in many places suggests that benthic organisms at the base of a toxic food chain grow well in areas recently denuded or disrupted by catastrophic events such as violent storms.

FISH	NO. OF INCIDENTS	REPORTED TOXIC		
		1934	1941	1958
jato (*Lutjanus vaigiensis* Quoy and Gaimard)	11	×	×	×
kuro (*Epinephelus fuscoguttatus* Forskal)	8	–	×	×
mijmij (*Lethrinus microdon* Cuvier and Valenciennes)	5	–	–	×
liele (*Rhinecanthus aculeatus* Linnaeus)	4	×	×	×
marea (identity questionable)	4	?	?	×
kur (identity questionable)	3	?	?	×
lane (*Caranx melampygus* Cuvier)	2	×	×	×
jawe (*Promicrops lanceolatus* Bloch)	2	×	×	×
kie (*Monotaxis grandoculis* Forskal)	2	×	×	×
yol (*Chelon vaigiensis* Quoy and Gaimard)	2	–	–	×
ikmouj (identity questionable)	2	?	?	×
lejebjeb (identity questionable)	2	?	?	×
malae (identity questionable)	2	?	?	×

TABLE 3

Toxic Fishes as Indicated by Fish Poisoning Episodes or Verbal Reports (1934, 1941, and 1958)

Marshallese Name	Scientific Name	Jaluit			Majuro
		1934 Matsuo*	1941 Hiyama*	1958	1958
Ban	*Lutjanus gibbus* (Forskal) *L. bohar* (Forskal)	+	+	+	+
Barot, baret	*Abudefduf septemfasciatus* Cuvier & Valenciennes	—	+	—	—
Bejerak	*Kyphosus* sp.	—	—	—	+
Betwettak	not known	+	+	+	—
Ikaboe molmol	*Scomber japonicus* Houttuyn	—	—	—	+
Ikbwij	*Caranx lessonii* Cuvier & Valenciennes *Trachinotus bailloni* (Lacépède)	+	+	+	+
Ikmouj	*Scarus harid* Forskal	—	—	+	+
Ikuit	*Plectropomus leopardus* (Lacépède)	+	—	—	—
Ilmok	*Gerres baconensis* Evermann & Seale	—	—	—	+
Jab, jato	*Lutjanus bohar* (Forskal) *L. vaigiensis* (Quoy & Gaimard) *L. gibbus* (Forskal)	+	+	+	+
Jalia	*Lethrinus miniatus* (Schneider)	+	+	+	—
Jawe	*Promicrops lanceolatus* (Bloch) *Plectropomus truncatus* Fowler	+	+	+	+
Jo	*Mulloidichthys auriflama* (Forskal)	—	—	—	+
Jome	*M. samoensis* (Gunther)	+	—	+	+
Jujukip	*Sphyraena picuda* Bloch & Schneider *S. forsteri* Cuvier & Valenciennes	+	+	+	—
Julae	*Plectropomus oligocanthus* Bleeker	+	+	+	—
Jure	*Sphyraena barracuda* (Walbaum)	+	+	+	—
Katak	not known	+	+	+	—
Kie, kielotan	*Monotaxis grandoculis* (Forskal)	+	+	+	+
Kuban	*Hepatis triostegus* (Linnaeus)	—	—	+	—
Kuro	*Epinephelus fuscoguttatus* (Forskal)	—	+	+	+
Lane, deltokrok	*Caranx melampygus* Cuvier & Valenciennes	+	+	+	+
Laum	*Aprion virescens* Valenciennes	—	+	—	—
Lejebjeb	*Epinephelus* sp.	—	—	—	+
Lemejine	not known	+	—	+	—
Liele, bub	*Rhinecanthus aculeatus* (Linnaeus)	+	+	+	+
Malle	*Siganus puellus* (Schlegel)	—	—	—	+
Mamennie	*Lethrinus* sp.	+	+	+	—
Mera, alowor	*Scarus jonesi* (Streets)	—	+	+	+
Mijmij	*Lethrinus microdon* Cuvier & Valenciennes	—	—	—	+
Momo	*Epinephelus macrospilos* (Bleeker)	—	—	—	+
Net	*Lethrinus variegatus* Cuvier & Valenciennes	—	+	—	—
Pelak, Berak	*L. kallopterus* Bleeker	—	—	—	+
Rewa	*Caranx fulvoguttatus* (Forskal)	—	—	—	+
Tiebro-ael	*Acanthurus nigricans* (Linnaeus)	—	+	+	+
Ulinno, Ilino	not known	+	+	+	—
Yol	*Chelon vaigiensis* (Quoy & Gaimard)	—	—	—	+
	Total	18	21	22	23

* *See* References.

PRESENT KNOWLEDGE OF FISH POISONS

Ciguatera

Fish most commonly incriminated in ciguatera are barracuda and snappers, although various reef fishes such as sea bass, groupers, and many others have frequently been implicated (Halstead, 1959). Symptoms in humans vary greatly, but usually appear in 1–10 hr. Numbness of lips and mouth occurs first, followed by tingling of the lips and extremities. Initial symptoms sometimes include a metallic taste, nausea, vomiting, abdominal cramps, and diarrhea. Generally the victim becomes extremely weak and prostrate, and in extreme cases muscular aches and pains are pronounced. Temperature sense may be reversed so that hot objects feel painfully cold and cold objects hot. A general inability to coordinate muscular movements may develop, and paralysis, muscular aches, and itching sensations may persist for several weeks or even months. In severe cases, complete recovery from weight losses, sensory disturbances, and weakness may require several years.

Recent research by Hashimoto (1956), Banner and Boroughs (1958), and McFarren and Bartsch (1960) indicates that barracuda poison and snapper poison are similar and perhaps identical. The poison is insoluble in water but is soluble in 90 per cent ethanol and certain other solvents, including acetone and diethyl ether. Beyond the knowledge that it will withstand boiling and is soluble in certain organic solvents, its chemical, pharmacological, and physical properties are still to be investigated.

Because of the recent discovery that ciguatera poison is not soluble in water, and because of possible toxic effects of salt in the extracts, much of the past assay data on ciguatera poison is questionable. Shortage of cats and the questionable validity of the mouse injection test led Banner and Boroughs to use the imported mongoose. Feeding tests with this animal showed it to be an acceptable test animal. They also noted that mice fed toxic fish were less sensitive to ciguatera poison than cats or mongooses. However, a successful assay may be done by injecting oil from a concentrated ether extract of the cooked fish into mice (McFarren and Bartsch, 1960).

Puffer Poison

Efforts by Japanese workers since 1909 have resulted in useful methods for extraction, purification, and characterization of puffer poison, known as tetrodotoxin (Tahara, 1910, Yokoo and Morosawa, 1955; Tsuda *et al.*, 1958; Tsuda and Kawamura, 1952*a*, *b*, 1953). In human cases the onset of symptoms is generally rapid and violent (Halstead, 1958). Malaise, pallor, dizziness, paresthesia of the lips and tongue, and ataxia frequently develop in 10 to 45 min. Hypersalivation, profuse sweating, extreme weakness, headache, subnormal temperature, decreased blood pressure and a rapid weak pulse also appear early. Nausea, vomiting, and diarrhea may or may not occur. The paresthesia may subsequently involve the fingers and toes and finally other parts of the body, causing victims to complain of feeling as if they are floating. Respiratory distress becomes prominent, and muscular twitching, tremor, and incoordination become progressively worse. With approaching death, the eyes become fixed and glassy, and convulsions occur. The victims usually remain conscious and mentally acute. Death results from respiratory paralysis usually in 6 to 24 hr.

Japanese workers assay the poison in dilute acetic acid and/or methanol and generally use subcutaneous injection, whereas recent studies (McFarren and Bartsch, 1960) indicate that puffer poison can be assayed in much the same manner as paralytic shellfish poison.

Moray Eel Poison

Practically no information is available concerning the chemical or pharmacological properties of moray eel (*Gymnothorax*) poison. Similarity of symptoms with those of ciguatera suggests a common poison (Randall, 1958) but it is now known that ciguatera poison is not water-soluble, whereas gymnothorax poison probably is. In studying gymnothorax poisoning, Ralls and Halstead (1955) used water or methanol acidified to pH 4.0 with acetic acid to obtain extracts for injection into mice. Appearance of prompt symptoms including hypoactivity, respiratory distress, convulsions, and death by respiratory arrest strongly suggest a water-soluble gymnothorax poison; water extracts

from ciguatera-producing species are not known to cause such symptoms. Although puffer poison also is water-soluble, symptoms of gymnothorax poison do not seem identical to puffer poisoning. As with ciguatera and puffer poisoning, the initial symptoms of gymnothorax poisoning may include tingling and numbness about the lips, tongue, hands, and feet, sometimes followed by nausea, vomiting, a metallic taste, diarrhea, and abdominal pain, as in ciguatera. The characteristic signs of gymnothorax poisoning, however, appear to be the absence of thoracic respiration, with pronounced abdominal breathing, profuse perspiration, excessive mucus production, purposeless movements, violent convulsions, and an extended period with absence of reflexes. Rapid respiration, rapid pulse, and high fever may develop. Khlentzos (1950) has reported dizziness, blurred vision, tremors of the hands, sensory changes in the legs, interosseous atrophy, muscular weakness, ulnar palsy, foot drop, radial weakness, deviation of the tongue, and a loss of voice probably due to laryngospasm. In severe intoxication, death did not occur until after 14 to 25 days.

Scombroid Poison

Recent Japanese studies (Kawabata *et al.*, 1955*a, b, c,* 1956) have shown that scombroid poisoning is an allergy-like food poisoning caused by the presence in the incriminated fish of an unusual amount of histamine and another more powerful vagus stimulant, called saurine. Large amounts of histamine and saurine are not naturally present in fish but apparently are produced by the action of certain strains of the bacterium, *Proteus morganii,* under conditions giving no obvious signs of putrefaction. Susceptible fishes are tuna, mackerel, bonita, and skipjack.

Isolation of saurine was accomplished by paper chromatography of a crude methanol extract leached from minced fish (probably *Cololabis saira* Brevoort). The newly isolated vagus stimulant was clearly differentiated from histamine and was tentatively named saurine. Saurine is insoluble in ether, acetone, benzene, chloroform, and absolute alcohol, although easily extracted with 80 per cent alcohol.

The physiological and pharmacological actions of saurine were determined by skin reactions in rabbits, shock symptoms in guinea pigs, and antagonism against anti-allergic drugs. These studies indicated that saurine has an additive effect to histamine and is different from acetylcholine. In humans, ½ to 2 or 3 hr. usually elapse after eating deteriorated scombroid fishes before appearance of symptoms, which include reddening of the face and the upper half of the body, exanthema like those of allergy, severe headache, and palpitation. Fever and diarrhea may accompany the illness in a few cases, and victims may become nauseated but rarely vomit.

PLAN FOR STUDY

Information now available emphasizes the need for further intensive and long-range studies of fish poisoning. Comprehensive studies will yield information of value to all places presently involved and eventually will also benefit areas other than those now known to be affected. Continuing epidemiologic studies should be intensified and coordinated with biochemical and biological approaches. Only by such an approach are significant advances likely within a reasonable period. Six principal phases are recommended:

1. Collection and analysis of epidemiologic data should be devised to observe incidence trends and establish more clearly the relationship of symptoms with species of fishes involved, their origin, and mode of handling. At present, considerable confusion surrounds the relationship of potentially toxic fishes to illness in humans. No systematic analysis exists of any large series of cases to indicate how many types of poisoning there actually are. Symptoms may be numerous and varied, and therefore a controlled analysis of clinical observations relating them to species and laboratory studies is of paramount importance. Fish poisoning incidence trends also should be evaluated in relation to weather, water characteristics, and other environmental phenomena in an effort to detect any significant influences they may have.

2. Because treatment of victims at present is only symptomatic and involves a multiplicity

of medications, a phase of study should be devoted to developing more effective therapy. The Trust Territory is now pursuing this objective.

3. To obtain toxic fish specimens for study, advantage should be taken of the normally occurring fish poisoning episodes among Marshallese and other populations in poisonous fish areas. In past studies the general procedure has been to collect hundreds of fishes and test all of them for toxicity by an assay procedure of some kind. Such costly and time-consuming effort to obtain one or two toxic specimens is exceedingly inefficient. Information thus obtained can only relate toxicity to the response in test animals, and it fails to provide the more important knowledge of human symptoms in response to the toxin of a specific fish. No investigator thus far has established a systematic procedure that will provide simultaneously pertinent information on symptoms in humans, knowledge of the causative fish's environment, symptoms in laboratory animals fed a part of the same specimen used for other analyses, and a record of human patient responses to a given therapy.

4. Because present assay procedures are inadequate, a simple on-the-spot test must be developed to determine if a fish is safe to eat, and to relate the quantity of poison present in a fish to the quantity that will cause human illness.

5. For a more rational approach to diagnosis and therapy and a better understanding of the biological activity of fish toxins, pharmacologic studies are needed to determine the physiologic response of test animals to fish toxins, and their mode of action. Studies will require large quantities of poisonous fish material, collection of which will pose difficulties.

6. The formation of toxins in fishes appears to be a response to some influence in the environment, perhaps involving feeding habits and susceptibility of the fish species. No way is known to predict toxicity in fishes at a given locality. Ecologic study is proposed to determine if there is some dependable relationship between one or more identifiable variables in the environment and the appearance of toxic fishes. If such relationships are discovered, poisoning episodes could be prevented by avoiding susceptible groups of fishes accordingly, or possibly by controlling the causes of toxicity.

ACKNOWLEDGMENT

Much of the information about fish poisoning in the Marshall Islands was taken from a report (Bartsch *et al.*, 1959) prepared at the request of the Trust Territory. The kindness of Mr. Delmas H. Nucker, High Commissioner of this agency, in permitting free use of the report material is appreciated. The writers also wish to acknowledge the assistance of Dr. William M. Ingram of the Robert A. Taft Sanitary Engineering Center, Cincinnati, Ohio, who made many helpful suggestions on the content of this paper.

REFERENCES

BANNER, A. H., and H. BOROUGHS. 1958. Observations on toxins of poisonous fishes. Proc., Soc. Exper. Biol. & Med. 98: 776–778.

BARTSCH, A. F., R. H. DRACHMAN, and E. F. MCFARREN. 1959. Report of a Survey of the Fish Poisoning Problem in the Marshall Islands. BSS. 117 pp.

BERLIN, R. 1948. Hoff disease in Sweden. Acta Med. Scand. 129: 560.

BENSON, JEROME. 1956. Tetraodon (blowfish) poisoning. J. Forensic Sciences 1: 119–125.

COURVILLE, DONOVAN A., BRUCE W. HALSTEAD, and DONALD W. HESSEL. 1958. Marine biotoxins: Isolation and properties. Chemical Reviews, pp. 235–248.

HALSTEAD, BRUCE W. 1951. A medical-military problem. Research Reviews, Office of Naval Research, pp. 10–16.

——— 1954. A note regarding the toxicity of the fishes of the skipjack family, Katsuwonidae. Calif. Fish & Game 40: 61–63.

——— 1958. Poisonous fishes. PHR 73: 302–312.

——— 1959. Dangerous Marine Animals. Cornell Maritime Press, Cambridge, Md. 146 pp.

——— and Norman C. Bunker. 1954. A survey of the poisonous fishes of Johnston Island. Zoologica 39: 61–77.

——— and Donald W. Schall. 1955. Report on the poisonous fishes captured during the Woodrow G. Krieger Expedition to the Galapagos Islands. In: Essays in the Natural Sciences in Honor of Captain Allan Hancock, Univ. of Southern Calif. Press, Los Angeles, pp. 147–172.

Hashimoto, Yoshiro. 1956. A note on the poison of a barracuda, *Sphyraena picuda* Bloch & Schneider. Bull. Japan. Soc. Scientific Fisheries 21: 1153–1157.

——— and M. Migita. 1951. Quantitative analysis method for fugu (puffer) toxin. Bull. Japan. Soc. Scientific Fisheries 16: 341–346.

Hiyama, Yoshio. 1943. Poisonous Fishes of the South Seas. [In Japanese.] Translated by W. G. Van Campen, in: Special Scientific Report, Fisheries No. 25, U.S. Dept. Interior, Fish & Wildlife Service, Washington, D. C., 1950.

Hori, Hiroyoki. 1957. Histopathologic study of crystalline tetrodotoxin, Report No. 1. Observation on acute intoxication in the mouse. Annual Report, Inst. Food Microbiology, Chiba University, Japan 10: 70–71.

Kawabata, T., K. Ishizaka, and T. Miura. 1955*a*. Studies on the allergy-like food poisoning associated with putrefaction of marine products, I. Episodes of allergy-like food poisoning caused by "samma sakuraboshi" (dried seasoned saury) and other kinds of marine products. Japan. J. Med. Sci. & Biol. 8: 487–501.

——— ——— ——— 1955*b*. Studies on the allergy-like food poisoning associated with putrefaction of marine products, II. Separation of causative substance and some of its chemical characteristics. Japan. J. Med. Sci. & Biol. 8: 503–519.

——— ——— ——— 1955*c*. Studies on the allergy-like food poisoning associated with putrefaction of marine products, III. Physiological and pharmacological action of "saurine," a vagus stimulant of unknown structure recently isolated by the authors, and its characteristics in developing allergy-like symptoms. Japan. J. Med. Sci. & Biol. 8: 521–528.

——— ——— ——— and T. Sasaki. 1956. Studies on the food poisoning associated with putrefaction of marine products, VII. An outbreak of allergy-like food poisoning caused by "sashimi" of *Parathunnus mebachi* and the isolation of causative bacteria. Bull. Japan. Soc. Scientific Fisheries 22: 41–47.

Khlentzos, Constantine T. 1950. Seventeen cases of poisoning due to ingestion of an eel, *Gymnothorax flavimarginatus*. Am. J. Trop. Med. 30: 785–793.

Matsuo, Ryuichi. 1934. Report of an investigation of poisonous fishes at Jaluit I. In: Collected Medical Reports on Endemic Diseases of the South Sea Islands, 2nd ed., South Seas Office, pp. 309–326. [In Japanese.]

McFarren, Earl F. 1959. Report on collaborative studies of the bioassay for paralytic shellfish poison. J. Assoc. Offic. Agri. Chemists 42: 263–271.

——— and A. F. Bartsch. 1960. Application of the paralytic shellfish poison assay to poisonous fishes. J. Assoc. Offic. Agri. Chemists 43: 548–554.

Murtha, E. F., D. E. Stabile, and J. H. Wills. 1958. Some pharmacological effects of puffer poison. J. Pharm. Exper. Thera. 122: 247–254.

Paetro, Sidney. 1956. Food poisoning caused by the great barracuda. PHR 71: 933–938.

Ralls, R. J., and B. W. Halstead. 1955. Moray eel poisoning and a preliminary report on the action of the toxin. Am. J. Trop. Med. & Hyg. 4: 136–139.

Randall, John E. 1958. A review of ciguatera, tropical fish poisoning, with a tentative explanation of its cause. Bull. Marine Science, Gulf and Caribbean 8: 236–267.

SCHWIMMER, M., and D. SCHWIMMER. 1955. The Role of Algae and Plankton in Medicine. Grune & Stratton, Inc., New York City. 85 pp.

SMITHSONIAN INSTITUTION. 1944. Survival on Land and Sea. Publications Branch, Office of Naval Intelligence, U.S. Navy.

TAHARA, Y. 1910. Uber das Tetrodon-Gift. Biochem. Ztschr. 30: 255–275.

TSUDA, K., and M. KAWAMURA. 1952*a*. The constituents of the ovaries of globefish, VI. Purification of globefish poison by chromatography. J. Pharmaceutical Soc. Japan 72: 187–190.

——— ——— 1952*b*. The constituents of the ovaries of globefish, VII. Purification of tetrodotoxin by chromatography. J. Pharmaceutical Soc. Japan 72: 771–774.

——— ——— 1953. The constituents of the ovaries of globefish, VIII. Studies on tetrodotoxin. Pharmaceutical Bull., Pharmaceutical Soc. Japan 1: 112–113.

——— ——— and R. HAYATSU. 1958. On the constitution of tetrodotoxin. Chemical & Pharmaceutical Bull. 6: 225–226.

YOKOO, A., and S. MOROSAWA. 1955. Studies on the toxin in globefish, No. 5. Comparison with tetrodotoxin. J. Pharm. Soc. Japan 75: 235–236.